AMENDMENT UNDER 37 C.F.R. § 1.111 Attorney Docket No.: Q87423

Application No.: 10/531,874

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

1. (currently amended): A method for treating obesity in a mammalian subject, which comprises administering to a mammalian subject in need of reduction of body weight an effective amount of a 15-keto-16-mono or dihalogen prostaglandin E_1 compound as shown by the following formula (I) Formula (II) to reduce body weight:

$$R_1$$
—A

 R_1 —A

 R_1 —A

 R_1 —A

 R_1 —A

$$R_1$$
—A
 X_1, X_2
 $B-Z-C-R_2-R_3$

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wherein L is oxo and M is hydrogen or hydroxy, and the five-membered ring may have one or more double bonds;

A is -CH₂, or -CH₂OH, -COCH₂OH, -COOH or a salt, ether, ester or amide thereof;

B is single bond, -CH₂-CH₂-, -CH=CH-, -C=C-, -CH₂-CH₂-, -CH=CH-CH₂-, -CH=C

Z is



 X_1 and X_2 are hydrogen, lower alkyl, or halogen, provided that at least one of X_1 and X_2 is halogen;

R₁ is a saturated or unsaturated bivalent lower or medium aliphatic hydrocarbon residue, which is unsubstituted or substituted with halogen, alkyl, hydroxy, oxo, aryl selected from the group consisting of phenyl, tolyl and xylyl which is unsubstituted or substituted or heterocyclic group selected from the group consisting of furyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, imidazolyl, pyrazolyl, furazanyl, pyranyl, pyridyl, pyridazinyl, pyrimidyl, pyrazinyl, 2-pyrrolinyl, pyrrolidinyl, 2-imidazolinyl, imidazolidinyl, 2-pyrazolinyl, pyrazolidinyl, piperidino, piperazinyl, morpholino, indolyl, benzothienyl, quinolyl, isoquinolyl, purinyl, quinazolinyl, carbazolyl, acridinyl, phenanthridinyl, benzimidazolyl, benzimidazolinyl,

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benzothiazolyl and phenothiazinyl which is unsubstituted or substituted, and at least one of carbon atom in the aliphatic hydrocarbon is optionally substituted by oxygen, nitrogen or sulfur;

R₂ is a single bond or lower alkylene; and

R₃ is lower alkyl, lower alkoxy, lower alkanoyloxy, cyclo(lower)alkyl, cyclo(lower)alkyloxy, aryl, aryloxy, heterocyclic group or heterocyclic-oxy group; wherein L, M and N are hydrogen atom, hydroxy, halogen atom, lower alkyl, hydroxy(lower)alkyl, lower alkanoyloxy or oxo, wherein at least one of L and M is a group other than hydrogen, and the five membered ring may have at least one double bond;

A is -CH₂, or -CH₂OH, COCH₂OH, COOH or a salt, ether, ester or amide thereof;

B is single bond, CH₂-CH₂-, -CH=CH , -C=C , -CH₂-CH₂-, -CH=CH-CH₂ , -CH₂
CH=CH , -C=C CH₂-or -CH₂-C=C ;

Z is C=O:

R₁ is a saturated or unsaturated bivalent lower or medium aliphatic hydrocarbon residue, which is unsubstituted or substituted with halogen, alkyl, hydroxy, oxo, aryl selected from the group consisting of phenyl, tolyl and xylyl which is unsubstituted or substituted or heterocyclic group selected from the group consisting of furyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, imidazolyl, pyrazolyl, furazanyl, pyranyl, pyridyl, pyridazinyl, pyrimidyl, pyrazinyl, 2-pyrrolinyl, pyrrolidinyl, 2-imidazolinyl, imidazolidinyl, 2-pyrazolinyl, pyrazolidinyl, piperidino, piperazinyl, morpholino, indolyl, benzothienyl, quinolyl, isoquinolyl, purinyl, quinazolinyl, carbazolyl, acridinyl, phenanthridinyl, benzimidazolyl, benzimidazolinyl,

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benzothiazolyl and phenothiazinyl which is unsubstituted or substituted, and at least one carbon atom in the aliphatic hydrocarbon is optionally substituted by oxygen, nitrogen or sulfur; and

Ra is a saturated or unsaturated lower or medium aliphatic hydrocarbon residue, which is unsubstituted or substituted with one or more substituents selected from the group consisting of halogen, oxo, hydroxy, lower alkoxy, lower alkanoyloxy, cyclo(lower)alkyl, eyelo(lower)alkyloxy, aryl, aryloxy, heterocyclic group and heterocyclic-oxy group; lower alkoxy; lower alkanoyloxy; cyclo(lower)alkyl; cyclo(lower)alkyloxy; aryl; aryloxy; heterocyclic group; or heterocyclic-oxy;

wherein said treating comprises care, relief, attenuation, or arrest of progression of obesity.

- 2. (canceled).
- 3. (canceled).
- 4. (canceled).
- 5. (currently amended): The method as described in Claim 1, wherein said $\underline{15\text{-keto-16-mono}}$ or dihalogen prostaglandin $\underline{E_1}$ compound is a 13,14-dihydro-15-keto-16-mono or dihalogen-prostaglandin $\underline{E_1}$ compound.
 - 6. (canceled).

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7. (currently amended): The method as described in Claim 1, wherein said $\underline{15\text{-keto-}}$ $\underline{16\text{-mono or dihalogen}}$ prostaglandin $\underline{E_1}$ compound is a 13,14-dihydro-15-keto-16-mono or difluoro-prostaglandin $\underline{E_1}$ compound.

- 8. (canceled).
- 9. (canceled).
- 10. (canceled).
- 11. (currently amended): The method as described in Claim 1, wherein said $\underline{15\text{-keto-16-mono}}$ or dihalogen prostaglandin $\underline{E_1}$ compound is a 13,14-dihydro-15-keto-16,16-difluoro-prostaglandin $\underline{E_1}$ compound or 13,14-dihydro-15-keto-16,16-difluoro-18-methyl-prostaglandin $\underline{E_1}$ compound.
- 12. (original): The method as described in Claim 1, which comprises systemic administration 1-4 times per day or continuous administration at the amount of $0.01\text{-}100~\mu\text{g/kg}$ per day.
- 13. (original): The method as described in Claim 12, wherein the administration is at the amount of $0.1-10 \mu g/kg$ per day.
 - 14. (canceled).
 - 15. (canceled).
 - 16. (canceled).

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- 17. (canceled).
- 18. (canceled).
- 19. (canceled).
- 20. (canceled).
- 21. (currently amended): A method for reducing body weight in a mammalian subject which comprises administering to a mammalian subject in need of treatment for obesity an effective amount of a 15-keto-16-mono or dihalogen prostaglandin \underline{E}_1 compound as shown by the following-formula (I) Formula (II) to reduce body weight:

$$R_1$$
—A

 R_1 —A

 R_1 —A

 R_1 —A

wherein L, M and N are hydrogen atom, hydroxy, halogen atom, lower alkyl, hydroxy(lower)alkyl, lower alkanoyloxy or oxo, wherein at least one of L and M is a group other than hydrogen, and the five-membered ring may have at least one double bond;

A is -CH₂, or -CH₂OH, -COCH₂OH, -COOH or a salt, ether, ester or amide thereof;

B is single bond, CH₂-CH₂-, CH=CH-, -C=C-, -CH₂-CH₂-CH₂-, -CH=CH-CH₂-, -CH₂-

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Z is C=0;

R₁ is a saturated or unsaturated bivalent lower or medium aliphatic hydrocarbon residue, which is unsubstituted or substituted with halogen, alkyl, hydroxy, oxo, aryl selected from the group consisting of phenyl, tolyl and xylyl which is unsubstituted or substituted or heterocyclic group selected from the group consisting of furyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, imidazolyl, pyrazolyl, furazanyl, pyranyl, pyridyl, pyridazinyl, pyrimidyl, pyrazinyl, 2 pyrrolinyl, pyrrolidinyl, 2 imidazolinyl, imidazolidinyl, 2-pyrazolinyl, pyrazolidinyl, piperidino, piperazinyl, morpholino, indolyl, benzothienyl, quinolyl, isoquinolyl, purinyl, quinazolinyl, carbazolyl, acridinyl, phenanthridinyl, benzimidazolyl, benzimidazolinyl, benzothiazolyl and phenothiazinyl which is unsubstituted or substituted, and at least one carbon atom in the aliphatic hydrocarbon is optionally substituted by oxygen, nitrogen or sulfur; and

Ra is a saturated or unsaturated lower or medium aliphatic hydrocarbon residue, which is unsubstituted or substituted with one or more substituents selected from the group consisting of halogen, oxo, hydroxy, lower alkoxy, lower alkanoyloxy, cyclo(lower)alkyl, eyelo(lower)alkyloxy, aryl, aryloxy, heterocyclic group and heterocyclic-oxy group; lower alkoxy; lower alkanoyloxy; cyclo(lower)alkyl; cyclo(lower)alkyloxy; aryl; aryloxy; heterocyclic group; or heterocyclic-oxy;

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$$R_1$$
—A
 X_1 X_2 (III)
 $B-Z-C-R_2-R_3$

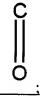
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wherein L is oxo and M is hydrogen or hydroxy, and the five-membered ring may have one or more double bonds;

A is -CH₃, or -CH₂OH, -COCH₂OH, -COOH or a salt, ether, ester or amide thereof;

B is single bond, -CH₂-CH₂-, -CH=CH-, -C=C-, -CH₂-CH₂-, -CH=CH-CH₂-, -CH=CH-CH₂-, -CH₂-CH₂-CH₂-, -CH=CH-CH₂-, -CH₂-CH₂-, -CH₂-, -CH₂

 \underline{Z} is



 X_1 and X_2 are hydrogen, lower alkyl, or halogen, provided that at least one of X_1 and X_2 is halogen;

 R_1 is a saturated or unsaturated bivalent lower or medium aliphatic hydrocarbon residue, which is unsubstituted or substituted with halogen, alkyl, hydroxy, oxo, aryl selected from the

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group consisting of phenyl, tolyl and xylyl which is unsubstituted or substituted or heterocyclic group selected from the group consisting of furyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, imidazolyl, pyrazolyl, furazanyl, pyranyl, pyridyl, pyridazinyl, pyrimidyl, pyrazinyl, 2-pyrrolinyl, pyrrolidinyl, 2-imidazolinyl, imidazolidinyl, 2-pyrazolinyl, pyrazolidinyl, piperidino, piperazinyl, morpholino, indolyl, benzothienyl, quinolyl, isoquinolyl, purinyl, quinazolinyl, carbazolyl, acridinyl, phenanthridinyl, benzimidazolyl, benzimidazolinyl, benzothiazolyl and phenothiazinyl which is unsubstituted or substituted, and at least one of carbon atom in the aliphatic hydrocarbon is optionally substituted by oxygen, nitrogen or sulfur;

R₂ is a single bond or lower alkylene; and

R₃ is lower alkyl, lower alkoxy, lower alkanoyloxy, cyclo(lower)alkyl, cyclo(lower)alkyloxy, aryl, aryloxy, heterocyclic group or heterocyclic-oxy group;

wherein said treating comprises care, relief, attenuation, or arrest of progression of obesity.

- 22. (canceled).
- 23. (canceled).
- 24. (currently amended): The method as described in Claim 1, wherein said $\underline{15\text{-keto-16-}}$ $\underline{\text{mono or dihalogen prostaglandin } \underline{E_1}$ compound is a 13,14-dihydro-15-keto-16-mono or dihalogen-prostaglandin El compound.
- 25. (currently amended): A method for treating obesity in a mammalian subject, which comprises administering to a mammalian subject in need of reduction of body weight an

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effective amount of <u>a compound which is</u> 13,14-dihydro-15-keto-16,16-difluoro-<u>PGE1 PGE1 or a</u> salt, ether, ester or amide thereof to reduce body weight, wherein said treating comprises care, relief, attenuation, or arrest of progression of obesity.

26. (new): The method according to Claim 25, wherein the compound is 13,14-dihydro-15-keto-16,16-difluoro PGE₁.